From the Department of Molecular Medicine and Surgery Section of Orthopaedics and Sport Medicine

Assessment of 3D movements in the Lumbar and Cervical spine with a new CT based method

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To
My Family

ABSTRACT

Background: Numerous methods for measuring segmental motion in spine have been described. However, because of the inaccessibility of the spine and the complexity of segmental movements, most of the noninvasive methods in use today have low accuracy or are unable to detect movements in all three cardinal axes. Almost all *in vivo* methods used for analysing segmental motion are based on two-dimensional (2D) radiographic examinations. Radiostereometris Analysis is so far the most accurate method to detect three-dimensional (3D) motion.

Specific aim: To develop and evaluate a non-invasive method for motion analysis of the spine using computed tomography (CT).

Methods: We studied segmental motion in a custom-made spine model, healthy subjects, and a small series of patients operated with total disc replacement. The subjects and patients were examined in flexion and extension on a fourth generation spiral CT unit. Analyses of the segmental movements in lumbar and cervical spine were done with a in-house developed software tool.

Results: In the lumbar spine the accuracy was 0.6 mm for translation and 1 degree for rotation in the model study. Movements of more than 1 mm could be visual detected. The repeatability on healthy subjects was 2.8 degrees in rotation and 1.8 mm in translation in vertebral segment. The mean facet joint 3D movement was for the right 6.1 mm and for the left 6.9 mm in L4-L5 segment and for the L5-S1 segment for the right facet 4.5 mm and 4.8 mm for the left. Mean rotation in the sagittal plane was 14.3 degrees in L4-L5 and 10.2 degrees in L5-S1. In patients with total disc replacement the mean rotation in the sagittal plane at the operated level (L5-S1) was 5.4 degrees before surgery and 6.8 after surgery. In the adjacent level (L4-L5) the mean rotation (degrees) was 7.7 before and 9.2 after surgery. The 3D translation in the operated level the left facet was 3.6 mm before and 4.5 mm after surgery and for the right facet joint 3.4 mm before to 3.6 mm after surgery.

In the cervical spine the accuracy was 0.7 degrees in rotation and 0.5 mm in translation in the model study. The repeatability on the model was 1.1 degrees in rotation and 0.3 mm in translation. The repeatability on patients was 2.3 degrees in rotation and 1.4 mm in translation. The median movement for the patient was in the sagittal plane for rotation 6.28 and translation 0.1mm, coronal plane 1.68 and 0.6 mm, and for the transverse plane 1.38 and 0.6 mm in translation

Conclusion: We have developed a non-invasive CT based method to study the 3D segmental movement in the spine. It has been tested in a model study, on healthy subjects and on patients with total disc replacement in cervical and lumbar spine. We believe that this method for detecting movements in the spine is useful both in research and for clinical use.

LIST OF PUBLICATIONS

Svedmark P, Weidenhielm L, Németh G, Tullberg T, Noz ME, Maguire GQ Jr, Zeleznik MP, Olivecrona H. Model studies on segmental movement in lumbar spine using a semi-automated program for volume fusion *Comput Aided Surg. 2008 Jan 13(1):14-22*

Svedmark P, Tullberg T,Noz ME, Maguire GQ, Zeleznik MP,Weidenhielm L, Németh G, Olivecrona H. Three-dimensional movements of the lumbar spine facet joints and segmental movements: in vivo examinations of normal subjects with a new non-invasive method. *European Spine Journal E-pub 1 sep 2011*

Svedmark P, Berg S, Noz ME, Maguire GQ, Zeleznik MP, Weidenhielm L, Németh G, Olivecrona H. Assessment of 3D movements in lumbar facet joints and segmental rotation of vertebrae with a new method in patients before and after TDR. *Submitted for publication*

Svedmark P, Lundh F, Németh G, Noz ME, Maguire GQ, Zeleznik MP, Olivecrona H. Motion analysis of total cervical disc replacements using Computed Tomography. Preliminary experience with nine patients and a model. *Accepted for publication in Acta Radiologica Scandinavia*

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LIST OF ABBREVIATIONS

CT	Computed Tomography
CTDR	Cervical Total disc Replacement
DCRA	Distortion compensated roentgen analysis
DDD	Degenerative disc disease
MRI	Magnetic resonance imaging
ROM	Range of motion
QMA	Quantitative motion analysis software
RSA	Radiostereometric analysis
THA	Total hip arthroplasty
TDR	Cervical Total disc Replacement
VAS	Visual Analogue Scale
2D	Two-dimensional
3D	Three-dimensional

1 INTRODUCTION

The spine is a complex structure; it consists of vertebrae and the interconnecting soft tissue. It has to provide strength, mobility, and stability. To achieve all these requirements, there are spine-specific properties for each spinal component, as well as the effective integration of these components into the overall structure of the spine. A “motion segment” consists of two vertebrae and the connecting soft tissue surrounding it. The mobility of these segments is defined by the range of motion (ROM) in normal conditions (i.e., during the movements of flexion-extension) and rotation in the sagittal plane. This mobility can be assessed in terms the change in the angle formed by two opposite vertebral endplates and translation in the sagittal plane. ROM depends on several factors, for example, age, degeneration, segment level, and pain (1). In extension, the main stabilizing structures are the anterior longitudinal ligament, the anterior part of the disc, the facet joints, and the rectus abdominis muscle (2). In forward flexion the movement is controlled by the posterior ligaments (interspinous and supraspinous ligaments), the facet joints and their capsules, the disc, and the paraspinal muscles(3). For side-bending movements, which are accompanied by some rotation with sliding separation of the facet joints, the inter transverse ligaments probably play an important role (4). Rotational movements are mainly controlled by the intervertebral disk and the facet joints(4, 5). Most studies to understand the segmental motion are made *in vitro,* for example we can find more than 1200 articles utilizing cadavers or animals. *In vivo* studies of the segmental movement of the spine are difficult. There are several different methods that have been applied for these *in vivo* studies, although radiographic techniques are the most common there are other methods, for example drilling rods/pins into the vertebra or the less traumatic placing of skin markers above the vertebras. It is important that the method(s) used have a high accuracy and a good precision so that the interpretation of the findings is correct.

1.1 RADIOGRAPHIC AND OTHER IMAGING METHODS

1.1.1 Lateral radiographs

Lateral radiographs allow measurement of the sagittal translation of a vertebra and vertebral rotation in the sagittal plane (flexion-extension). This is the most common method for assessing segmental motion in the sagittal plane. However, there are many errors that can occur when using this method. The main sources of error in measuring translation and rotation in the sagittal plane are: the technique used to measure translation, the quality of the radiographs, and the concomitant rotation in the sagittal plane (i.e., sagittal rotation) and/or rotation about the vertical axis of the spine (i.e., axial rotation). Shaffer et al. (6) showed these sources of error in a phantom study where the L4-L5 segment had a fixed angulations and translation and where radiographs with different quality and with different concomitant rotation of the segment. Since there are several different methods of measuring the segmental movement on lateral radiographs, seven different methods were used for evaluation. These studies on those methods suggest that high consistency and accuracy in a ideal experimental situation does **not** ensure false-positive and false-negative rates in clinical use. When concomitant motion is involved, even relatively large measured translations may occur when the actual translations are substantially smaller. Even with high-quality radiographs, minimal (<5 mm) translations may be overestimated, while less often more substantial translations (>5 mm) are overestimated. Panjabi et al.(7) evaluated the accuracy of plain radiographs and reported an accuracy of 4 mm in translation. Lim et al.(8) reported on total disc replacement (TDR) that in order to be 95% certain that an implanted TDR prosthesis has any sagittal motion, a ROM of at least 4.6° must be observed, which is the upper limit of intra observer measurement variability for a TDR with a true ROM of 0°. For this reason ROM measurement variability should be considered when evaluating the success or failure of motion preservation in lumbar TDR.

The use of computer software for evaluating the lateral radiographs is a method that has shown to increase the accuracy of ROM measurements. There are several methods, but here we will discuss only the DCRA and the QMA methods as they currently seem to be the most interesting for the moment.

Distortion-compensated X-ray analysis (DCRA) is a method for measuring rotation and translation in the sagittal plane from lateral radiograph of the spine. The method is based on identifying the vertebral contours in lateral view and of geometric measurements that are virtually independent of distortion, axial rotation or lateral tilt, and determining the pattern of translational and rotational motion, to implement on a protocol based on these geometric measures. It was first described by Frobin et al. (9) who reported an accuracy of 1.6 degrees and 1.2 mm in translation in the sagittal plane. This is a much higher accuracy than the most other radiograph methods used until that time. Leivseth et al. (10) compared DCRA with RSA and found an error in the L5-S1 at 2.3 degrees and about 1.6 mm in translation lumbar spine. There is a similar study in the cervical spine (11) with similar results.

Quantitative motion analysis software (QMA) (QMA, Medical Metrics Inc, Houston, TX) The QMA software has the ability to measure intervertebral rotation and translation in the sagittal plane of flexion / extension radiographs (12, 13). It claims that the software algorithm accounts for the effects of out-of-plane magnification, and poor visibility in the endplates. Zhao et al (14) have shown that this method has a accuracy to 0.8 mm in translation and 0.6 degrees of rotation which is a is a great improvement over other 2D methods(15). Park et al. (16) did a comparing study of Cobbs and QMA with RSA in patients with TDR. They did not see any significant difference between QMA and digital Cobb technique but it was a greater variation was found between these techniques and RSA. This indicates that the lateral X-rays of the variation in patient positioning or in the direction of the X-ray beam can result in a 10% -15% variations in the estimated range of vertebral displacement.

1.1.2 Bi planar X-ray

The 3D reconstruction of the spine in upright posture can be obtained by bi-planar radiographic methods developed since the 1970s (17). The principle is to simultaneously take orthogonal X-rays, then manually or with the aid of a computer identify 4–25 anatomical landmarks per vertebrae in the images in both projections. Following the identification of these landmarks three-dimensional (3D) movements can be calculated. Pearcy et al. (18) reported in 1985 an accuracy of 2 mm and 1.5 degrees of rotation. Orthogonal X-rays can be combined with magnetic resonance images to increase accuracy and precision (19). However, there have been some problems determining anatomic landmarks on bi-planar radiographs.

Additionally, this method’s complexity and the requirement for special equipment makes this method difficult to use in routine clinical setting.

Radiostereometric analysis (RSA) has the ability to measure 3D movements in the spine (19, 20) with very high accuracy. It was developed in the 70 th by Selvik (12). This method is invasive, it requires the insertion of tantalum markers in each vertebra to create ridged bodies. Two x-ray tubes angled 40° to each other are necessary to generate simultaneous exposures of the patient's tantalum-marked vertebrae together with a calibration cage (containing tantalum markers in well-defined positions) placed between the patient and the film plane (13, 14). RSA has proven to be a precise method for evaluating motions between different structures and has been used in many orthopedic fields, such as prosthetic fixation(15), joint stability and kinematics(16), and spinal fusion stability(17, 18)
The RSA accuracy determined from the results of repeated radiographic examinations has a accuracy of 0.7°, 0.2°, and 0.3° for rotatory motion around the transverse, vertical, and sagittal axes and of 0.2 mm for translatory motion along these axes (21, 22). RSA has proved to be the best method to detect very small movements between vertebrae. Unfortunately, this method is technically difficult, time consuming, and requires specific apparatus. Moreover, because of its invasive nature, it is unsuitable for studies involving large numbers of patients

1.1.3 Computer Tomography (CT)

Tomography of x-ray pictures was one of the pillars in radiology before CT was invented. It was presented in the early 1900s by the Italian radiologist Alessandro Vallebona. Exploiting the availability and computational performance of minicomputers and their introduction of the transverse axial scanning method. Godfrey Hounsfield and Allen Cormback pioneer CT scanning. They shared the Nobel Prize in 1979 for the invention of computer tomography (CT). The first EMI-Scanner was installed in Atkinson Morley Hospital in Wimbledon, England, and the first patient brain-scan was done on 1 October 1971(30) based upon 160 parallel readings per scan and with each scan taking a little over 5 minutes. The images was then processed in a large computer (at those days) for 2,5 hours to reconstruct the volume. The first and second generation of CT scanners acquired one slice at time (Single slice CT scanners) using either a pencil or a fan beam, a single detector and a combination of rotation and translational movements. Third and fourth generation of CT scanners allow the gantry to rotate while the couch with the patient moves without stopping. (These are referred to as Spiral or Multislice CT scanners) The third generation used a fan x-ray beam and smooth rotation of the x-ray tube and detector array while fourth generation CT scanners have rotational motion of the x-ray tube within a stationary circular array of detectors of 600 or more detectors. The development of CT scanners, with their improved spatial resolution in both axial and longitudinal plane, has enabled a transition from evaluating individual CT images to assessing entire CT volumes, either in 2D or in 3D. Software in the CT scanners used today have also reduced, though not yet eliminated, the image artifacts caused by metal; thus imaging of prostheses is becoming more and more feasible. Today, 30 years after the first clinical CT image, it is difficult to name a hospital without at least one CT scanner. Lim et al(31) developed a three-dimensional imaging technique using parallel computed tomography (CT) scans to determine rotations and translations in individual cadaveric cervical vertebrae. The authors illustrated that accurate measurements (±1 mm and ±1°) can be made using CT in vitro. Orchia e al(32, 33) expanded this technique to measure vertebral segmental rotations and translations, in human lumbar spines *in vivo*. One of the major problems with CT scans is the high radiation dose compared to ordinary x-ray. With the new generation of CT machines it has been possible to lower the radiation dose significant. Abdul-Kasim et al(34) has created a low dose protocol for scoliosis that is almost the same as for ordinary scoliosis X-rays. In our method we are also using a low dose protocol.

1.1.4 Magnetic Resonance Imaging (MRI).

MRI is the latest method of detecting pathology in the spine. MRI is routinely performed with the patients supine and with no possibility to provoke the patient due to limited tunnel space. Recent advances in MRI machines such as improvement of magnets and coils have made the development of open MRI systems possible. Recent studies have used such open MRI systems as they provide sufficient volumes for the evaluation of the lumbar spine under upright weight-bearing conditions in either seated or standing body positions (35, 36). Flexion-extension provocation in the seated position is difficult for the patient and it is difficult to exactly match the volumes, thus the results are not really convincing. Despite continuous development of MRI equipment, essential problems still arise during attempts to perform examinations in upright posture for patients with spinal disorders (37, 38).

1.1.5 Other measurement methods

Other methods for measuring *in vivo* spinal movements involve trading off noninvasiveness for accuracy and comprehensiveness. These methods include noninvasive goniometers (39, 40) and skin-mounted optical (41) or electromagnetic (42) markers. These methods provide ready but imprecise data (40). More invasive methods include the insertion of Kircher wires into the spinous processes in the lumbar spine. Electromagnetic tracking sensors can be attached to these wires. Using this method Steffen et al.(43) showed an error of only 0.5 degrees and 0.7 mm in translation. However, such an invasive method is of course not an option for larger studies.

1.2 TOTAL DISC REPLACEMENT (TDR / CTDR)

Total disc replacement in cervical spine (CTDR) or in lumbar spine (TDR) involves replacement of the intervertebral disc with an artificial articulation between the vertebral bodies. The main goal of this operation is to reduce pain, while trying to restore or preserve segmental movement and stability. TDR is performed with a disc prosthesis, that has two endplates and between these an articulation where either metal articulates to polyethylene (as in many hip- and knee-prostheses) or there is a metal-to-metal articulation. The design of these prostheses is either a “non-constrained” center of mobility or a “semi-constrained” one. The non-constrained design features a mobile core that articulates with both endplates, thus the center of rotation varies. The semi-constrained is more of a “ball and socket” design with a fixed center of rotation. In this thesis we evaluate both cervical total disc replacement and lumbar total disc replacement with our new method.

1.3 DIGITAL IMAGE REGISTRATION

Image registration has been widely used to compare aerial reconnaissance images. The process of registering digital images is based upon digital correlation or matching of two or more images spatially (geometrically), i.e., determining the correspondence between multiple digital image data sets. Basically, it is the process of transforming multiple data sets to same position, hence bringing the co-homologous points into corresponding (comparable) positions. This leads to the alignment of the data volumes in 3D or slices in 2D. This can be done between any two volumes or slices that have corresponding data points.

When applied to digital medical image data sets, these sets must represent the same part of the body. The data sets can be collected from different modalities or serially from the same modality. The registration can be accomplished between planar (2D) volumes, between tomographic (3D or nD) volumes, or between a planar and a tomographic volume. After image registration has been successfully performed, then various techniques allow these data sets to be integrated, merged, or 'fused', for display and other analysis.

In this work we have been using an image processing tool, developed together with Saya Systems Inc. (formerly, RADH Oncology Products). The registration algorithm incorporated in this tool has previously been extensively validated (44-50) and can be used to calculate an affine (including rigid body) or non-affine (using warping techniques) transformation in which the coefficients are derived from manually picked point pairs (landmarks).

In the studies described here, two or more computer tomography (CT) volume data sets were registered to bring these data sets into spatial alignment. The coordinates of the corresponding volume elements (voxels) from the different three dimensional data volumes were transformed aligning the landmarks, thus aligning the spatial coordinates of these data volumes. These volumes were then merged or fused for evaluation and further analysis. The methods used for accomplishing this are described in detail below.

2 AIMS

Overall aims: Studies included in the present thesis where part of a project to develop a non-invasive method for detecting segmental movements in the lumbar and cervical spine. The development was done as a series of four studies:

I	The aim of Study I was to evaluate the accuracy and the repeatability of segmental translation in different cardinal planes and in 3D in the lumbar spine, in a model study.
II	The primary aim of Study II was to assess 3D movement of the facet joints and the segmental rotation of the vertebrae in the lumbar spine in healthy subjects. A secondary aim was to assess the repeatability of the method and also to determine the accuracy of rotation using a phantom.
III	The aim of Study III was to apply the method to patients with total disc replacement. The assessment of the 3D movement of the facet joints and the segmental rotation of the vertebrae in the operated level L5-S1 and in the adjacent level L4-L5 were evaluated.
IV	The aim of Study IV was to extend this CT based method developed in the earlier studies for use in the cervical spine with a new algorithm for standard orientation of the vertebras. We evaluated the accuracy and repeatability of this improved method.

Each study is described in a separate paper. The papers (numbered I to IV corresponding to the four studies) can be found at the back of the thesis.

3 METHOD AND MATERIAL

3.1 SPINE PHANTOM

A phantom with two base plates incorporating three vertebrae was constructed. The phantom allowed orthogonal translations and rotations with six degrees of freedom. One segment of the model incorporated two vertebrae mounted along an axis collinear and rotatable around the model's x-axis. This segment was mounted so that it could be independently translated along the three cardinal axes of the model relative to the second model segment. The second segment incorporated one vertebra mounted so that it could be rotated around the model's z-axis and along the model's y-axis (given that the rotation around the z-axis was zero). Translations were achieved using screws with one millimeter of motion per revolution. Rotations were achieved using pairs of screws for the x- and y-axis rotation and around a rotating hinge for z-axis rotation. Rotations were monitored using graduated arcs. For study I and II, three lumbar vertebras were mounted. For study IV, three cervical vertebras were mounted and an artificial cervical disc replacement was incorporated in the moving segment (Discover artificial cervical disc, Depuy Spine, Inc., Taynham, MA, USA).

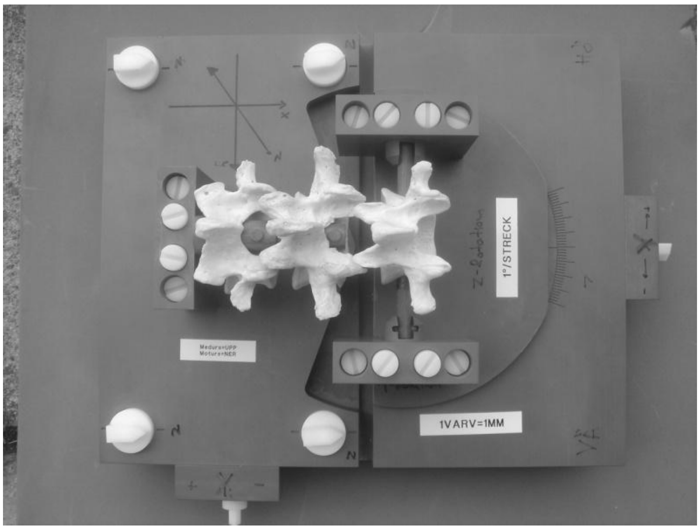


Figure 1: The model with three human lumbar vertebras

3.2 SUBJECTS AND PATIENTS

For study II, eleven asymptomatic healthy subjects with no prior history of back pain were recruited. For study III, ten patients with degenerative disc disease were recruited prior to lumbar total disc replacement surgery. For study IV, nine patients who had undergone primary cervical total disc replacement surgery were included.

3.2.1 Procedure for acquisition of CT volumes

CT volumes were acquired using the clinical scanners at our department. For studies I to III, a LightSpeed QX/I fourth-generation spiral CT unit (General Electric Medical Systems, Milwaukee, WI, USA) was used to acquire images with

1.25 mm collimation and a pitch of 3 (0.75 mm/rotation), at 250 mA, 120 kV. Images were reconstructed with 1.25 mm increments. For study I and II, the spine phantom was repeatedly scanned. For studies II and III, each subject´s (patient´s) lumbar spine was scanned twice. The subjects were placed on a custom made jig (OT-Center, Danderyd, Sweden) which provokes the lumbar spine into flexion or extension by using different blocks. A provocation of the spine was made in the supine position for extension and in the prone position for flexion.

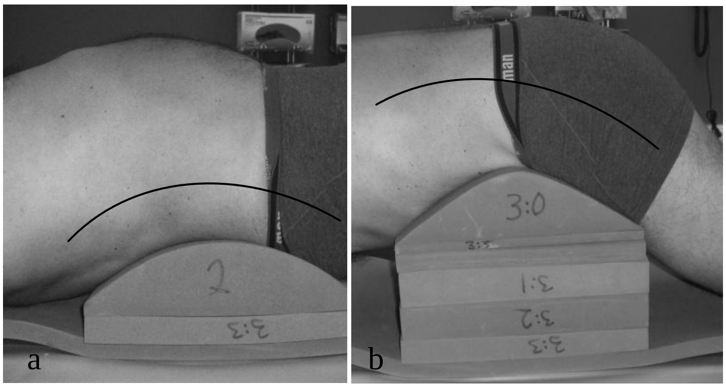


Figure 2. Provocation of the lumbar spine in extension(a) in supine position and flexion(b) in prone position.

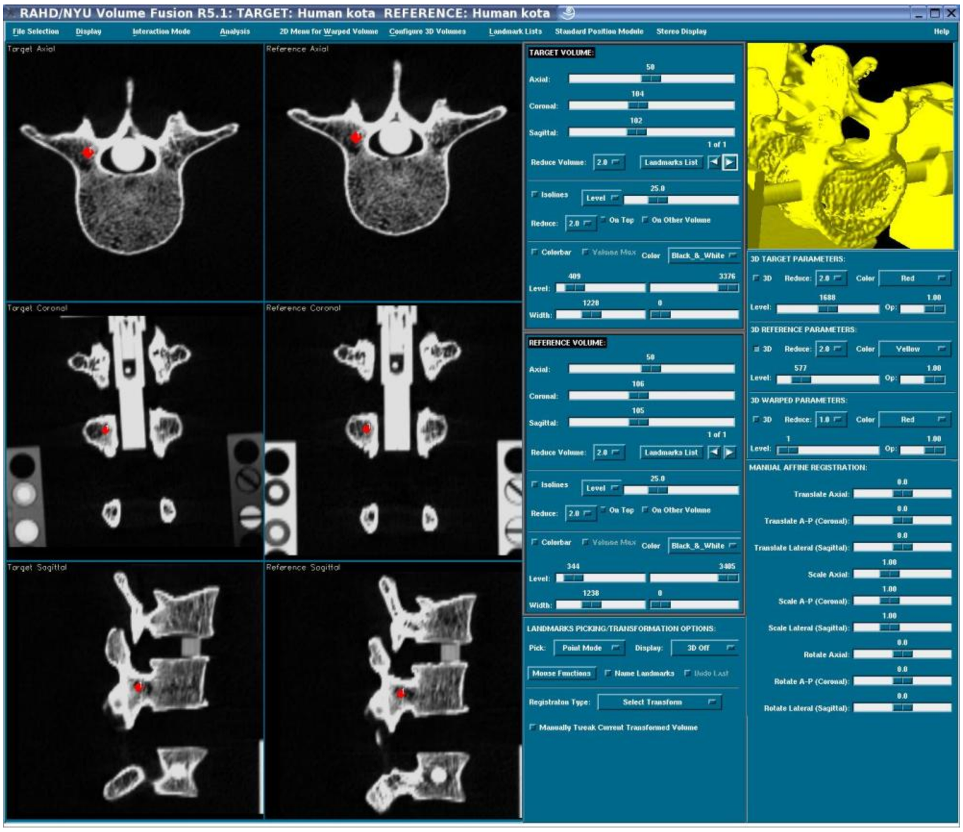
The radiation dose was calculated to be 0.68 mSv per scan. For study IV, the spine phantom was repeatedly scanned using a Lightspeed 16 CT unit (GE Healthcare, Wauskesha, WI, USA) used to acquire images with total collimation widthcm 20 and a pitch of 1.375, at 1.722mAs, 120 kV. The patients were scanned in flexion and extension of the cervical spine three months post-operatively using a Somatom Definition AS CT unit (Siemens, Erlangen, Germany) to acquire images with total collimation widthcm 12 and a pitch of 0.9, at 47mAs, 140 kV. The effective dose was calculated to 0.33 mSv per scan. The patients were placed in the CT scanner on their left shoulder at a 90 degree angle to the supine position. A stiff pillow supported the head and clinically the cervical spine was in a neutral position before the scans.

3.2.2 Tool for digital image registration, fusion, and analysis

The image-processing tool used in this study includes functionality for volume registration, fusion, and data analysis. It employs a Motif based user interface from which functions from IBM's Visualization Data Explorer (DX) software package (now available as open source software, http://opendx.org) are invoked. The DX software suite provides an object-oriented, graphical programming interface. The DX data model is discipline-independent (i.e., it can be used for any visualization application including medicine), self-describing, and supports regular and irregular grids with node and connection-dependent data. DX's very complete data model enables voxels to be localized within separate volumes in an N-dimensional space (here a three dimensional space). For further details visit the website http://sayasystems.com and click on "3D Volume Fusion" on the left hand side. While we have not solved all the possible registration problems, we have shown that, using the algorithms available in this tool and using information concerning anatomically corresponding point pairs, we can overcome many of the difficulties encountered in registering medical image volumes which are not initially well matched.

3.2.3 User interface

The image processing tool's user interface presents arbitrarily chosen slices from two volumes simultaneously (e.g., a reference and a target or the volume to be transformed), with optionally superimposed isolines of the user’s choosing. While either volume can be displayed on the left or the right, the volume displayed on the right is always considered the reference volume. Two larger views can be used to display slices in one of the three orthogonal planes or six smaller views can be used which present corresponding slices in all three planes (axial, coronal, and sagittal). Window width and level functionality is provided for viewing CT volumes. In the case of orthopedic prosthetic research (such as the work described in this thesis), this tool was adapted to have two window width and level settings in order to provide a lower window, which can be used for viewing the skeletal structure, and a higher window for simultaneously viewing metal or other highly attenuating structures. Simultaneously a 3D subsurface can also be displayed as a 3D shaded surface (isosurface). The 2D slices can be zoomed and/or panned for viewing a particular feature. The 3D volumes may also be zoomed, panned, and rotated for viewing particular features from an arbitrary direction



TARGET VOLUME:
Axial: 50
Coronal: 104
Sagittal: 102
1 of 1
Reduce Volume: 2.0
☐ Isolines Level 25.0
Reduce: 2.0 ☐ On Top ☐ On Other Volume
☐ Colorbar ☐ Volume Max Color Black_&_White
Level: 409 3376
Width: 1228 0

REFERENCE VOLUME:
Axial: 50
Coronal: 106
Sagittal: 105
1 of 1
Reduce Volume: 2.0
☐ Isolines Level 25.0
Reduce: 2.0 ☐ On Top ☐ On Other Volume
☐ Colorbar ☐ Volume Max Color Black_&_White
Level: 344 3405
Width: 1238 0

LANDMARKS PICKING/TRANSFORMATION OPTIONS:
Pick: Point Mode Display: 3D Off
☐ Name Landmarks ☐ Undo Last
Registraton Type: Select Transform
☐ Manually Tweak Current Transformed Volume

3D TARGET PARAMETERS:
☐ 3D Reduce: 2.0 Color Red
Level: 1688 Op: 1.00

3D REFERENCE PARAMETERS:
☑ 3D Reduce: 2.0 Color Yellow
Level: 577 Op: 1.00

3D WARPED PARAMETERS:
☐ 3D Reduce: 1.0 Color Red
Level: 1 Op: 1.00

MANUAL AFFINE REGISTRATION:
Translate Axial: 0.0
Translate A-P (Coronal): 0.0
Translate Lateral (Sagittal): 0.0
Scale Axial: 1.00
Scale A-P (Coronal): 1.00
Scale Lateral (Sagittal): 1.00
Rotate Axial: 0.0
Rotate A-P (Coronal): 0.0
Rotate Lateral (Sagittal): 0.0

Figure 3. Simultaneous display of two CT volumes (reference left and target right) in the three cardinal plans. A single landmark in the L4 vertebrae in each volume is shown (red diamond) on the orthogonal slices that intersect it.

3.2.4 Choosing Landmarks

The only interaction which must necessarily be performed by the user is to choose landmarks on concurrently viewed slices to assure the best match between the corresponding physiologic point or structure or (as implemented for this research) landmarks could be chosen directly on the 3D isosurface. The view of the slices may be moved up and down in the individual volumes. Landmarks can be selected in multiple planes simultaneously, i.e., in 2D the landmark in the reference slice can be chosen on the axial view, while the corresponding landamark is chosen on the sagittal view on the target slice. On the 2D slices, landmarks are chosen by clicking on a point with the pointer device, or with the aid of a 3D spherical landmark which can moved in 3D using the pointer device. The sphere's radius may be chosen by the user and/or resized interactively with the pointer device. The spherical landmark superimposes the contours of a three-dimensional sphere simultaneously on all three slices. When the spherical landmark is placed appropriately a landmark is generated from the 3D co-ordinates of the sphere's center. When a landmark is chosen the corresponding point in the 3D volume is recorded in distance units *independent* of any voxel's location, and a sequence number is automatically assigned. Additionally, the user can optionally automatically generate an out-of-plane landmark to break the symmetry if necessary, for example when using a rigid body transformation. This is particularly useful when performing analysis on the cervical spine.

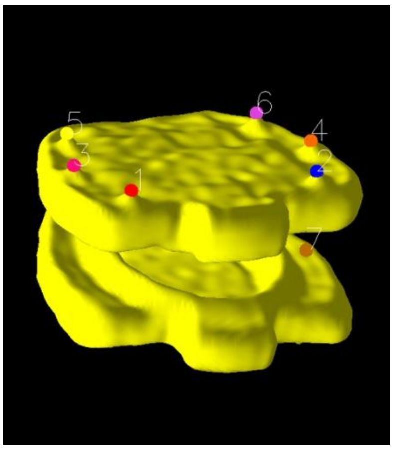


Figure 4. 3D isosurface display of CTDR in a patient. Six landmarks designated corresponding features on the back side on upper part of the prosthesis. The seventh point is automatically generated from three of the original points to maintain a consistent orientation

3.2.5 Volume Registration

To limit the effect of mismatched points and to generate transform coefficients for arbitrary volume data sets, a weighted least square linear regression is employed using the paired 3D landmarks. The eigenvalues of the matrix of coefficients are obtained by a Gauss-Jordan matrix inversion or by Singular Value Decomposition, depending upon the type of registration algorithm that is desired (i.e., a warping or rigid body transform). At present, the x, y, and z-coordinates are given equal weight in either transformation, although normally there is a much finer resolution in the x and y directions of the CT data when compared with the z direction. It is possible to weight the linear regression to compensate for this difference, but presently this is not done. Finally, a transformation is performed. This transformation may be **affine** (which preserves the original relationship between the structures involved, i.e., the straightness of lines, parallelism, and the ratio between the length of two segments of the same line, however, lines and angles may not be preserved - this can be used if the object is a rigid body) or **non-affine** (which has more degrees of freedom, line lengths and angles can change, straight lines can become curved, and does not preserve parallelism). Transformations may be first or second degree polynomial warps or rigid body transformations. A manual affine transformation is also available (providing only translation, rotation, and scaling). For the applications in the four studies of this thesis a rigid body transform was used. This type of transformation preserves the spatial integrity of structures involved. Note that rigid body transformations include only rotations and translations. Rotations about the three Cartesian coordinate axes x, y, z when combined with translations can orient the object anywhere in space. In a rigid body transformation only the position and orientation of the object will change. Rigid body transformations are Euclidean transformations; hence they preserve length and angle measure. A rigid body transformation is a subset of the affine transformations that do **not** include scale or shear. In the application described in this thesis, the angle measure in the form of the Euler angles and linear transformation associated with the rigid body transform are generated and saved in a comma-separated file for later reference.

3.2.6 Visual Verification

Once the newly transformed volume has been created from the original, untransformed data set, this new volume may be re-sliced identically to the reference volume and evaluated side by side with the reference volume, or superimposed on the reference slices, in any of the three planes. Further analysis can be accomplished by blending the images, using a 2D horizontal or vertical curtain, or using a re-sizable view port. An isosurface of the transformed volume may be displayed in 3D, and optionally an isosurface from the reference volume and/or the target volume can be superimposed for comparison. As before, this may be done in large or small display format and the volumes can be zoomed, panned, and rotated in order to be viewed from an arbitrary direction.

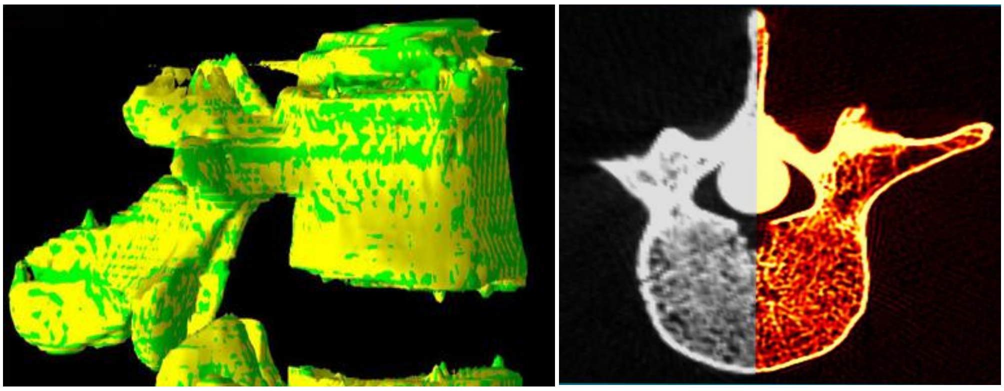


Figure 5. (a) A 3D display of L4 after registration. Note the overlapping.”zebra-like” pattern between the reference volume isosurface (yellow) and the transformed volume isosurface (green) created when the two surfaces coincide. This pattern indicates that the registration is better than the smallest image element (voxel) in the volumes. (b) A 2D overlay axial view where the gray (left) side of the vertebra is the reference volume and the red (right) side is an overlay. of the transformed volume on the

reference volume. Note the close match between all the condensed areas of the vertebrae

3.2.7 Further Analysis

The transformed volume may be saved and redisplayed as the target volume. The transformed volume may also be registered together with the reference volume either to create a better match, or if the match is considered adequate, to generate a numerical correlate of migration. In this thesis the latter is done by applying landmarks to corresponding structures in the image of the implanted components in the reference and transformed volume.

3.2.8 Statistical Verification

The program provides summary statistics and these statistics can be viewed by the user after the transformation has been done. These statistics include the distance between the reference landmark and the transformed target landmark in millimeters for each of the chosen landmarks. The original target landmarks are transformed exactly as the target volume was transformed. Additionally, the mean, standard deviation, and standard error of the mean are given for the set of landmark distance differences as well as minimum and maximum error distances. Optionally, the user may view the same set of values separately for each individual direction and also for the planar x-y direction.

3.2.9 Other modules

In conjunction with the adaptation of this tool for orthopedic research, a standard position module was first developed for total hip arthroplasty (THA) studies. The purpose for doing this was that this provided a very simple way to see how an orthopedic implant is implanted in relationship to the reference system by rotating the image from the standard position along the cardinal axes of the pelvis-cardinal axes of the screen and displaying numerical data about this rotation. If we know that the main axes of a pelvis is aligned with the screen's main axes, then simply rotating around the screen's superior-inferior axis until the cup is seen from the side corresponds to anatomic anteversion and a direct measurement of rotation around the screen's antero-posterior axis corresponds to the anatomic inclination. It should be noted that the current diagnostic tool, planar X-ray, has a precision of 5 degrees for these angles. The pelvis has a defined coronal plane (the McKibbin plane including the right and left spina iliaca anterior superior and the public tubercles). One way to achieve this position is to first place the axial view of the pelvis horizontally on the screen. In this position there is only one degree of freedom between the axes of the screen and the anatomic axes of the pelvis, which is the degree of rotation around the tangent axis of McKibbin-plane. By making an orthogonal 90 degree rotation around the screen's left-right axis, this McKibbin plane is placed parallel to the screen. Rotation around the screen's antero-posterior axis until the left and right tuber os ischii is horizontal locks this last degree of freedom yielding a standard position, with an anatomical frontal view of the pelvis. This was later adapted to place the spine into a standard position when viewed in the sagittal plane. However, this was a completely manual operation and required the user to perform a number of rotations in 3D. For the cervical spine work in this thesis, we devised first an algorithm where the standard position could be generated from three landmarks placed at specific positions in the volume. We later improved this so that the standard position was derived from eigenvectors generated from the original set of landmarks chosen for the volume registration. We then automated this process, so that once the registration landmarks were chosen, the registration and the subsequent analysis leading to the generation of the final Euler angles and translations were performed automatically.

3.2.10 Overview of statistics

In conjunction with each of the studies in this thesis, the error measurements performed on the landmarks by the tool described above were examined. These were used in conjunction with the visual verification describe above to determine that each specific registration was satisfactory.

The analytical results from each study were tested graphically to determine if they were normally distributed. A histograph, boxplot, density plot, and quantile-quantile normal plot were used. In each case the data was found to be mostly normally distributed with outliers shown, particularly in the boxplot and quantile-quantile normal plot. The Student's t-test was used to calculate if the data from the different tests were significantly different and to indicate the confidence interval. This calculation was confirmed by using a Wilcoxon Signed Rank Test with continuity correction. Accuracy and repeatability were tested according to methods outlined in (51, 52).

For paper four, an ANOVA (53) was also used to confirm that there were no interactions among the model results nor among the patient results with repect to the measurements being made. Additionally, the limits of agreement for all the data was calulated according to the method outlined in (54).

All the statistics were calculated using R version 2.11.1(55).

4 SUMMARY OF STUDIES AND RESULTS

4.1 STUDY I. MODEL STUDIES ON SEGMENTAL MOVEMENT IN LUMBAR SPINE USING A SEMI-AUTOMATED PROGRAM FOR VOLUME FUSION

The objective was to determine if volume registration with CT and our volume merging software tool was able to detect segmental movements in the lumbar spine. The study is a model study aiming to evaluate the accuracy both numerically and visually in all three cardinal axes. One hundred and four CT volumes were acquired of a custom made model incorporating three lumbar vertebrae. In the first 54 CT scan we used plastic vertebras. Since plastic vertebras themselves do not produce any “condense areas” we used tantalum bullets to simulate condensed areas. In the last 50 CT scans we used human vertebrae. Lumbar segmental translation was simulated by altering the position of one vertebra (L3) in all three cardinal axes between acquisitions. The CT volumes were combined into 64 case pairs, simulating lumbar segmental movement of up to 3 mm between acquisitions. Volume registration (described in section 3.2.5 on page 11) was done on each of these case pairs. Nine corresponding landmarks were placed in the L4 volumes “reference” and “target”. A ridged body transformation was carried out to align the volumes in the same coordinate system. The transformed volume is then re-sliced and a new set of nine corresponding landmarks on the reference volume and the transformed volume were selected in the L3 vertebrae. Calculation of the differences between the corresponding L3 landmarks between the reference volume and the transformed volumes were calculated and expressed as vectors. The average displacement of all nine landmarks was then calculated, along with the 3D distance and the distance along the cardinal axes.

4.1.1 Findings

Volume registration of the vertebrae could be attained in all cases. This was confirmed with 3D superimposed isosurfaces, where a specific “zebra-like” pattern is obtained when the isosurfaces coincide (Figure 5). Also when displayed as a 2D overlay inspection revealed an almost perfect match could be seen. Visual evaluation showed that starting from a perfect match a translation of 1.0 mm in any direction was visible as a clear color separation in the overlays and between the transformed and the reference volumes (Figure fig 6).

Numerical evaluation of the accuracy (for all cases) was for 3D 0.56 mm and for the cardinal axes the accuracy was: sagittal axis 0.45 mm, coronal axis 0.46 mm, and for the axial axis 0.45 mm. The repeatability (of 10 cases) was 0.35 mm.

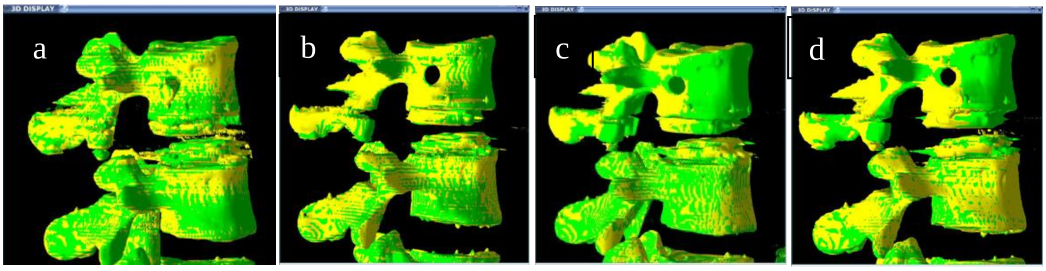


Figure 6. 3D isosurface displays after registration of L4. (a) A case with no movement. Note the “Zebra” pattern between reference (yellow) and the transformed vertebra (green) in both vertebras. In (b) 0.5 mm (c) 1.0 mm, (d) 2.0 mm there are a sagittal translation of the upper vertebra.

4.2 STUDY II. THREE-DIMENSIONAL MOVEMENTS OF THE LUMBAR SPINE FACET JOINTS AND SEGMENTAL MOVEMENTS: *IN VIVO* EXAMINATIONS OF NORMAL SUBJECTS WITH A NEW NON-INVASIVE METHOD

In this study we expanded this method from the model study to healthy subjects. Eleven healthy asymptomatic subjects with no history of low back pain were recruited from the hospital staff, five males and six females with a mean age of 35 years (28–49) and a mean BMI of 24.The subjects were placed on a custom made jig (OT-Center, Danderyd, Sweden), which can with different blocks provoke the lumbar spine into flexion or extension. A provocation of the spine was made in the supine position for extension and in the prone position for flexion (figure 2). Low back pain during examination was assessed using a Visual Analogue Scale (VAS). The subjects were gradually provoked in the jig up to maximal flexion or extension, but provocation was stopped if the low back pain was over 70 on the 100 VAS scale or if in the prone position the space between the top of the CT scanner tunnel and the subject’s spine was too small. The subjects underwent two CT scans, one in flexion provocation and one in extension provocation. Images were reconstructed with 1.25 mm slice thickness. The radiation dose was calculated to be 0.68 mSv per scan.

The measurements of movement in the spine between extension and flexion examinations were done with the same software as in study I. It was performed in two steps:

1. The two volumes were registered so that the volumes of the L5 vertebra in the flexion and extension acquisition were fused with ridged body transformation after placing nine corresponding landmarks in the L5 vertebras. After the transformation volumes were spatial align in the same coordinate system i.e. the entire volumes are now placed in the same coordinate system. The coordinate system was defined by the CT scanner and the origin of this system was located in the center of the CT volume. All rotations and translations were calculated in this system.
2. Facet joint translation and segmental rotation of L4 and S1 in respect to L5 where measured in the registered volumes.

In the second step we used these registered L5 volumes; by placing nine co-homologous landmarks in L4 and S1, respectively, spread in 3D for stability. In each facet joint we registered four landmarks that were spread as much as possible in the facet joint. To check that these landmarks are co-homologous we registered L4 and S1, respectively, and if this brought these vertebrae and facets into alignment, then (using our visual and numeric analysis as above) the landmarks were accepted. From the rotation matrix generated from the rigid body transformation we obtained the Euler angles by decomposing the matrix in the following order: $R_zR_yR_x$ where R_x is the rotation about the X-axis (i.e., the sagittal plane) and was applied first, into the cardinal axes of the vertebra L4 and S1 in relation to L5 and for facets the translation matrix generated from the rigid body transformation we obtained the 3D movement of the left and right facet joint in L4–L5 and L5–S1. This was expressed as the translation of the rigid body in 3D.

In this study we also used a model (the same model as used in study I) to determine the rotation accuracy. A set of 24 CT scans combined into different cases in order to calculate accuracy.

4.2.1 Findings

All subjects were able to extend and flex their spine in the jig with only moderate low back pain during examination. All the vertebras could be successfully recorded and analyzed. The mean 3D facet joint translation at L4–L5 was 6.1 mm (right) and 6.9 mm (left). At L5–S1 the facet joint translation was 4.5 mm(right) and 4.8 mm (left). The mean rotation at the L4–L5 level was 14.3 degrees (sagittal plane), 0.9 degrees (coronal plane), and 0.6 degrees (transverse plane) and at the L5–S1 level the mean rotation was 10.2 degrees (sagittal plane), 0 degrees (coronal plane), and 0.2 degrees (transverse plane).

Repeated analysis for 3D facet joint movement was on average 5 mm with a standard mean error of 0.6 mm and repeatability of 1.8 mm (with a 95% CI). For segmental rotation in the sagittal plane the mean rotation was 11.5 degrees and standard error of mean 1 degree. The repeatability for rotation was 2.8 degrees (with a 95% CI). The accuracy for rotation in the phantom was in the sagittal plane 0.7 degrees, coronal plane 1 degree, and 0.7 degrees in the transverse plane.

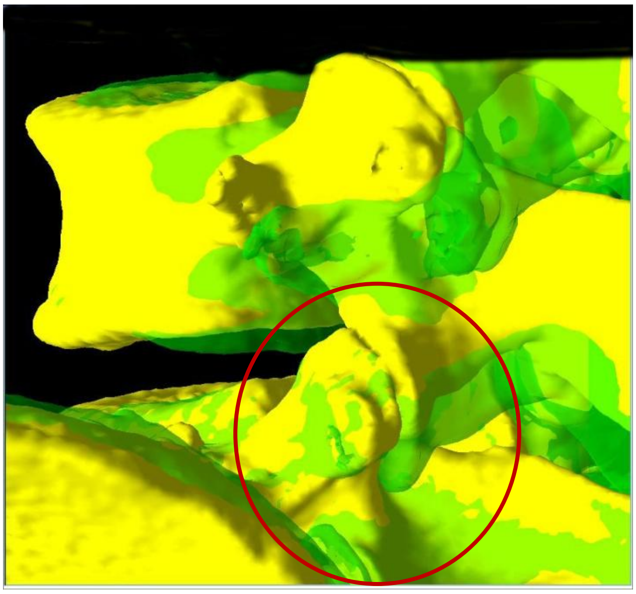


Figure 7. Left Facet joint movement in L4–L5 represented in 3D.flexion volume(yellow) and extension volume (green)

4.3 STUDY III. ASSESSMENT OF 3D MOVEMENTS IN LUMBAR FACET JOINTS AND SEGMENTAL ROTATION OF VERTEBRAS WITH A NEW METHOD IN PATIENTS BEFORE AND AFTER TDR

In this study we applied the method that had been developed in studies I and II to patients with degenerative disc disease (DDD) and who were selected for surgery for total disc replacement in the lumbar spine at the L5-S1 level. Ten patients were included in this study. Of these ten patients, five received Prodisc, three Charite, and two Maverick prostheses at the L5-S1 level. Each patient was examined before surgery and three years after surgery. Each examination consisted of two CT scans, one in provoked flexion, and one in provoked extension, with pain evaluated using the visual analogue scale (VAS). The flexion and extension CT data were then spatially registered in 3D, and then the segmental movement and facet joint translation were measured at the L4-L5 and L5-S1 levels.

4.3.1 Findings

All patients were able to extend and flex their spine in the jig before surgery and three years after surgery. The CT tunnel was large enough for provocation for all patients. Volume registration of the vertebrae was successful in all cases. Both segmental rotation and facet joint translation were effectively visualised in the registered volumes. In one case the prosthesis had subsided into the L5 vertebra, while in the other patients there were no large subsides or any bone bridges between the vertebras as a sign of spontaneous fusion. In the numeric analysis the mean value for error in all the landmarks in the vertebrae was 0.7 mm.

There was no significant difference in segmental rotation or in facet joint 3D translation between the preoperative provocation and the three years' post-operative provocation.

The median rotation in the sagittal plane at the operated level (L5-S1) was 5.4 degrees before surgery and 6.8 degrees after surgery. In the adjacent level (L4-L5) the median rotation (degrees) was 7.7 degrees before and 9.2 degrees after surgery. The 3D translation in the operated level the left facet was 3.6 mm before and 4.5 mm after surgery and for the right facet joint 3.4 mm before to 3.6 mm after surgery. The median VAS was reduced from 6 to 3 in extension and from 4 to 2 in flexion.

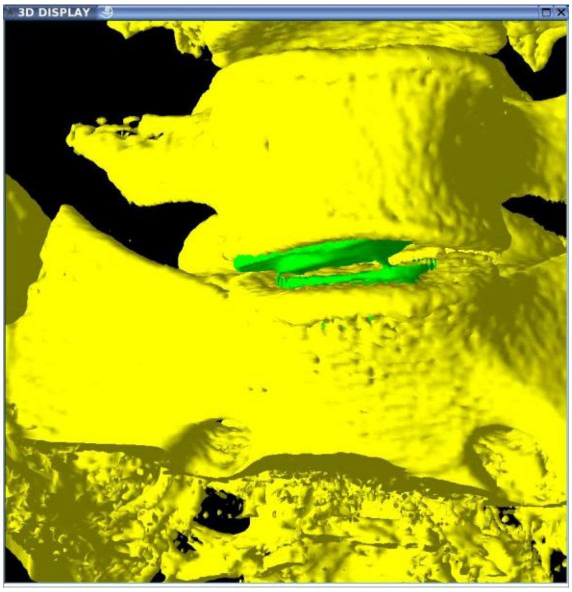


Figure 8. A 3D view showing the the disc prothesis (green) that has subside in tho the L5 vertebra.

4.4 STUDY IV. MOTION ANALYSIS OF TOTAL CERVICAL DISC REPLACEMENTS USING COMPUTED TOMOGRAPHY. PRELIMINARY EXPERIENCE WITH NINE PATIENTS AND A MODEL

In this fourth study, we moved from the lumbar spine up to the cervical spine. We examed nine patients with total disc replacement in the cervical spine, mean age 42 and age range: 38-56. Additionally, a model was constructed, incorporating three human cervical vertebrae and an identical cervical total disc replacement as used in the patients, which allowed orthogonal rotations around three axes. We used a new algorithm for the analysis in which we orientated each of the volumes into a standard orientation before we calculated the translation and Euler angles of rotation in all cardinal planes. Instead of landmarking the verterbae we landmarked the upper and the lower component of the prosthesis (see Figure 4) with each six landmarks.

The patients were scanned in flexion and extension of the cervical spine using a clinical CT scanner with a routine low-dose protocol (0.33 mSv). The flexion and extension CT volume data were spatially registered, and the prosthetic kinematics of two prosthetic components, an upper and a lower component, were calculated and expressed in Euler angles and orthogonal linear translations relative to the upper component. For accuracy and repeatability analysis, the model was scanned and processed in the same manner as the patients. The accuracy for the method was calculated using 45 cases. The repeatability study was made on 7 patients and on the model cases. We also created “pseudo model cases” (61 cases) to simulate different patients’ positioning between two different examinations in order to determine the stability of the method even if the spatial orientation of the prosthesis (note we are referring to the same spatial relationship between the upper and lower components of the prosthesis) had changed between the examinations.

4.4.1 Findings

All model scans could be used, but two patient volumes were unsuitable for analysis because the pegs on the backside of one of the prosthesis, due to partial volume effects, were too poorly visualized in 3D for reliably placing landmarks.

Analysis of both the model and patients showed good repeatability, i.e., within 2 standard deviations of the mean using the 95% limits of agreement with no overlapping confidence intervals. The accuracy analysis showed that the median error was close to zero.

Visual examination of all patient volumes did not show any peri-prosthetic osteolysis or any apparent movement between the prosthetic components and adjacent vertebrae, thus there were no signs of loosening.

The median movement for the patient was in the sagittal plane for rotation 6.2 degrees and 0.1 mm of translation, coronal plane 1.6 degrees and 0.6 mm of translation, and for the transverse plane 1.3 degrees and 0.6 mm of translation.

The repeatability analysis showed 95% of the values were within less than two standard deviations of the mean in accordance with the criterion given in(52).The repeatability is presented in Table 1. When the measured angle from the CT scans was compared with the rotations in the model the result was consistent and not dependent on the size of the angle. This was confirmed by the repeated CT scans and subsequent analysis

The accuracy with a 95% confidence interval in the model study was for the sagittal plane 0.7 degrees and 0.4 mm for translation, coronal plane 0.4 degrees and 0.2 mm, and for the transverse plane 0.2 degrees and 0.5 mm

Table 1.

95% Limits of Agreement on Two Trials - Repeatability								
	Patients				**Model**			
	Mean Difference	95% Upper Limit	95% Lower Limit	Repeatability	Mean Difference	95% Upper Limit	95% Lower Limit	Repeatability
Coronal (degrees)	-0.08	0.25	-0.41	0.47	0.04	0.49	-0.40	0.63
Sagittal (degrees)	-0.36	1.24	-1.95	2.25	-0.01	0.76	-0.78	1.09
Transverse (degrees)	-0.07	1.19	-1.32	1.78	0.01	0.66	-0.64	0.92
Coronal (mm)	-0.05	0.23	-0.33	0.40	0.01	0.21	-0.19	0.29
Sagittal (mm)	0.06	1.03	-0.90	1.36	0.00	0.13	-0.12	0.18
Transverse (mm)	0.06	0.27	-0.14	0.29	0.01	0.16	-0.14	0.22

5 DISCUSSION

The overall aim of this thesis was to develop and test a non-invasive CT based method for the assessment of segmental motion in the cervical and lumbar spine. Using this method, we studied the mechanics of segmental motion in a model in both healthy subjects and in patients with cervical and lumbar total disc replacements. A new software tool, adapted for spinal applications in orthopedic research was utilized. This tool, originally developed for inter-modality volume registration, was previously adapted for orthopedic applications and tested in total hip arthroplasty (THA) studies. Two dissertations from our group resulted from the THA studies (H.Olivecrona 2004, L Olivecrona 2010) and in elbow kinematics studies (Ericson 2010). In the process of developing and applying this tool to the spine we chose to start with the lumbar spine because the vertebras are larger and the soft tissues surrounding the vertebra are not as sensitive to radiation as in the case of the cervical spine.

In study I we showed that, using CT in conjunction with volume registration, it was possible to measure segmental translation in the spine with high accuracy, i.e., around 0.5 mm in all cardinal axes and 0.6 mm in 3D on a model. This method also allowed us to evaluate the motion visually in 2D and in 3D with an accuracy of around 1 mm. This visual evaluation was important in evaluating if the vertebrae were correctly matched and to help understand how the vertebra moved. This visual evaluation was especially important because numerical evaluation can be difficult to interpret, particularly when more complex spinal motions are studied. In the initial study we used plastic vertebras with tantalum marker beads, because the CT data of the plastic itself did not give us any suitable locations (equivalent to condense bone areas) due to the homologous structure on which to place landmarks. While finding and marking tantalum beads is more straight-forward than finding condense bone areas in the human vertebras, the quality of registration did **not** differ significantly between the plastic or human vertebras. For example, the mean error between the landmarks was 0.4 mm in this study and there were no differences between the plastic or human vertebras. The number of landmarks was set to nine. With nine landmarks it was possible to obtain a reasonable spread of the landmarks in three dimensions in the vertebras. Additional landmarks might create a more stable ridged body, but placing them would increase the workload for each fusion *without* a clear decrease in error. The segmental translation when it was not always aligned according to the CT coordinate plane could induce a small error when calculating the cardinal axes translation accuracy because a segmental translation induces a translation in two directions due to the different coordinate systems. On the other hand this segmental translation is a very small movement even though this problem existed the method had accuracy around 0.5 mm in all directions. This initial study was intended as a model study under ideal conditions. For example, the segmental coordinate system was manually aligned to be *almost* in alignment with the CT machine's coordinate system. This made it easier to find landmarks that were consistent between the volumes. On the other hand, the aim of the study was to determine if this method could be used for the spine and how well it could be performed in an ideal situation. There are many other methods with high accuracy in experimental situations, but when applied clinically are considerably less precise. Shaffer et al.(56) found that, even though this other methods have a high accuracy in a model situation, the errors were up to 5 mm in a clinical setting.

In study II we showed that it was possible to analyze image volumes of lumbar vertebras in healthy subjects in flexion and extension. We evaluated the movement in individual facet joints. To our knowledge, there is no other radiographic method for measurement of individual 3D movement of the facet joints that is clinically applicable. In our study, the facet's joint movement was symmetric for all subjects. The 3D magnitude is in the same level that has been reported in other studies (19). We reported repeatability for the method of 2.8 degrees and 1.8 mm in the lumbar spine. The repeatability study was made on both levels (L4-L5 and L5-S1) where L4-L5 had a repeatability of 2.8 degrees and L5-S1 had 2.0 degrees. We believe that the better repeatability in L5-S1 could be due to the sacrum being a larger bone which makes the corresponding rigid body larger and hence more stable or the fact that the ROM is smaller in the L5-S1 level. However, this was based upon a small series of subjects; therefore we chose to present the larger value for the repeatability for this method. The magnitude of the segmental movement is similar to other studies in L4-L5 (57), but somewhat smaller for L5-S1. This difference could be a result of difficulties in provoking the subject´s spine into full flexion in the supine position, due to the spatial limitations of the CT tunnel. This makes the method less applicable in larger patients; therefore we excluded patients with BMI above 35 for analysis with this method. When provoking the patient in flexion, the acquisition of the flexion volume is generally of somewhat lower quality, probably due to the fact that the spine is off-centered in the CT tunnel. We used a low-dose CT protocol with a calculated dose exposure of 0.68 mS. For comparison, a lateral lumbar X-ray exposes a patient to approximately 0.3-0.4 mS. However, most lumbar X-ray studies include four pictures (two lateral and two anterior-posterior views) adding up to be almost equivalent to the exposure for a pair of low-dose CT scans. In the future, with the advent of new CT hardware and software, it is likely that the radiation exposure can be decreased further while maintaining or increasing the precision using this method.

Study III comprises a small patient series to study total disc replacement (TDR) in L5-S1. Provocation and analysis were performed in the same way as in study II. It was interesting to see that the rotation of the segments, both at the adjacent and at the operated level, is about the same three year after surgery as it was before surgery *independently* of if the patient had a small or large rotation. On the other hand the patients had a significant lower pain on the follow up provocation exam. This result might indicate that TDR more or less preserves motion in the segment, but does not restore the segment motion altered by disease, but with lower pain during motion.. Studies from other groups confirm these findings (57); while yet other studies claim that TDR increases the mobility of the segment (58). It is of course important to be aware of the performance characteristics of the different radiographic methods used to evaluate the motion. Park et al. (16) reported a study comparing QMA and digital Cobb technique with RSA in patients after TDR. A large variability was seen *between* these techniques and RSA. Lim et al.(59) reported that to be 95% certain that an implanted TDR prosthesis has any sagittal motion, a ROM of at least 4.6° must be observed, which is the upper limit of intra-observer measurement variability for a TDR with a true ROM of 0°. In our study the 95%CI for repeatability was 2.8 degrees.

The facet joint movement was asymmetric defined to be more than 2 mm (the method repeatability 1.8 mm) in three patients before operation in the operated level. Two of these patients had symmetric facet joint movement in the follow up examination. However, in two other patients an asymmetric facet joint movement was induced. The patient with asymmetric movements before and after surgery showed large osteoarthritis in the left facet joint. For the other two patients, in whom surgery might have induced asymmetry of the facet joint movement; one had the prosthesis midline slightly off center from the midline of the vertebra. One of these patients had induced asymmetry of the facets joint but we failed to find any explanations except that the patient had the prosthesis that was least constrained in this small series. It might be the case that this prosthesis allows translation more than others prostheses. To evaluate how different types of disc prosthesis move we would have to do a much larger study and also develop a standard orientation of the segment so that we can express the cardinal translations of the facets joints in a standardized orientated coordinate system for all patients. There is already a possibility to express the cardinal translation in different planes, but since the volumes did not have a standard orientation the data may not be comparable between two examinations; therefore we chose to express the 3D magnitude of the movement of the facets instead - as this is comparable between different examinations. We did a smaller pilot study in which we tried to initially place the volumes into a standard position before placing landmarks on them, but the data showed that reconstructing the volumes into a matrix in this standard position lost too much clarity in the images due to the interpolation in the reconstruction algorithm. To overcome this problem would require new protocols for acquisition without increasing the radiation dose of the CT volumes with a reduction in the slice thickness from the current 1.25 mm to 0.6 mm. These thinner slices would probably increase the precision in the lumbar spine of this method.

In study IV we examined the cervical spine. An improved new algorithm was introduced for finding the standard position of the vertebras. All the landmarks were designated in the original volumes, and then an automated process moved the volume into a registered and standard orientation and position, in which segmental rotations and translations were calculated. The study was conducted on both a custom made model and on 9 patients. The accuracy study for the method in a model situation was around 1.0 degrees for rotation and 0.5 mm in translation in the different axes. Repeatability for these patients was 2.3 degrees for rotation and 1.4 mm for translation. To our knowledge, there is no other non-invasive 3D method with this accuracy and precision in the cervical spine. Some limitations of this method in the cervical spine should be noted. We use the pegs of the prosthesis for landmarking (figure 4). These pegs are 1 mm high and the slice thickness was 1 mm in the patients. The head was supported by a soft pillow during provocation. This combination of factors caused partial volume effects, resulting in two cases in the pegs of the prosthesis being too poorly visualized in 3D for reliably placing landmarks. Consequently we were not able to analyze these two patients in this study. We have now changed to a stiff pillow and are using a new algorithm that computes eigenvectors for the standard orientation (see method& material) and a slice thickness of 0.6 mm. These changes have eliminated the problems that had been observed in two patients that we were not able to analyze. In an ongoing study in the cervical spine with 29 CTDR patients, where we intend to do double examinations and inter/intra observer evaluation, we have so far done double examinations (test-re-test) in the CT scanner with flexion and extension provocations on nine patients and all volumes were successfully analyzed and without the problems described above. The repeatability for the double examinations with a 95% CI is 2.8 degrees and 2.0 mm. These preliminary results match those reported by Zoega et al. using RSA(60). However, they are not as good as Lind et al.(61) reported when looking at a Bryan Prosthesis with the RSA technique.

In this thesis we have described a new CT-based non-invasive method for the detection of 3D motion of the lumbar and cervical spine. We have used model studies, healthy subjects and patients in order to evaluate this method. We have evaluated accuracy and repeatability of the lumbar and cervical spine for this method. There are some limitations and risks to this method that has to be addressed. The use of CT scans exposure the patients to radiation, even though we use low-dose protocols. Another limitation is the provocation, the difficulties to maximal provocation especially in flexion, and for patients with high BMI. The problem of standard orientation of the lumbar spine limits to some extent the evaluation of cardinal segmental movements. On the other hand the strength of this method is that it can express the 3D magnitude of the individual facet joint and as we know there is no other non-invasive 3D method that expresses that. Another strength of our method is the fact that it can be used clinically and can be done on any be done on any modern CT machine. Future development of CT machines will probably increase this methods accuracy and precision. We believe that our method is well suited for to assess kinematics of the spine in order to address clinically relevant issues

6 CONCLUSIONS

These four studies present a new CT based method combined with volume registration of CT data for assessing the lumbar and cervical spine. We showed that this method for detecting 3D segmental movements in the cervical and lumbar spine has both a high accuracy and repeatability. The segmental movement can both be analyzed visually and quantified numerically in all three axes. With a low dose CT scanning protocol the radiation dose is almost as low as for acquiring 2D data using ordinary planar X-rays. We believe that this method of detecting movement in the spine is useful both in research and for clinical use.

I. The accuracy and repeatability for translation in the model was high. The precision for visual evaluation was good. This method seems to be suitable to study segmental movement in the lumbar spine.

II. The method could assess the translations of the individual facet joints and segmental rotation of the vertebrae in different planes. The repeatability was 2.8 degrees in rotation and 1.8 mm in translation which we considered to be good. The accuracy for rotation was high in the phantom study.

III. We showed that our method was suitable to study patients operated with total disc replacement in the lumbar spine. We could assess segmental rotation and translation in the operated level and in the adjacent level in all patients.

IV. In conclusion, this study has shown a non-invasive CT based method for detecting 3D segmental movements in the cervical spine after CTDR with both high accuracy and repeatability. The segmental movement can both be analyzed visually and quantified numerically in all three axes.

7 CLINICAL IMPLICATIONS AND FUTURE STUDIES

In an ongoing study on cervical spine segmental motions, so far nine patients have done test and retest examinations. The results are very promising and are almost in the level with RSA in the cervical spine. Our method is also suitable for evaluating stability in patients with cervical or lumbar spine fusion. Persistent pain in the spine after fusion surgery could be due to instability (or over-mobility) of the fused segment. In some cases there are difficulties to accurately diagnose this instability. In an ongoing pilot study so far with 12 patients enrolled, all with persistent pain one year after fusion our method detected five patients with instability. In those patients conventional radiographic examination did not detect this instability. The method can be improved by introducing auto-detection and in the lumbar spine, standard orientation. This will improve the ability to compare kinematics of different implants and make the analysis faster.

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8 SUMMARY IN SWEDISH

Bakgrund: Ryggsmärta är ett vanligt problem i befolkningen. Orsaken till ryggsmärtan är för det mesta okänd men degeneration av mellankotsskivan som skapar förutsättningar för onormal rörlighet mellan kotorna med åtföljande smärta anses vara en tänkbar förklaring till ryggsmärta. Kirurgisk behandling av detta tillstånd med steloperation i ryggen är en etablerad metod. På senare år har ersättning av den degenererade mellankotsskivan med en sk diskprotes också blivit ett alternativ. Ryggen har en komplex mekanisk struktur. Den är sammansatt av sk kotsegment dvs två kotor med mellanliggande mellankotsskiva och omgivande mjukdelar. I kotsegmentet sker rörelser. Dessa rörelser består av en kombinations av vrid- och glidrörelser då kotorna rör sig i förhållande till varandra i rymden. Hos levande människor utförs vanligen en röntgenundersökningen i frontal- och sidoplanet för att bestämma kotornas inbördes läge i segmentet. Detta är en tvådimensionell undersökning som kan bestämma kotornas läge i det undersökta planet med hög precision men inte förmår att detektera kotornas tredimensionella rörelser med särskilt hög precision. Den metod som hittills använts för att studera kotornas tredimensionella rörelser med hög precision *in vivo* är röntgenstereofotogrammetri. Metoden innebär att man först sätter in metallkulor i ryggkotorna och sedan röntgar patienten med två vinkelräta projektioner samtidigt. Genom matematisk databehandling av metallkulornas läge kan man sedan fastställa den tredimensionella rörelsen mellan kotorna med hög precision. Metoden lämpar sig för forskning där man studerar små patientserier men inte som klinisk rutinmetod. Det finns således behov av att utveckla en klinisk rutinmetod som kan detektera kotornas tredimensionella rörelser med hög precision.

Specifikt mål: Att utveckla och utvärdera en icke-invasiv metod för tredimensionell segmentell rörelseanalys av länd och nack ryggraden med hjälp av datortomografi

Metod: Vi studerade segmentell kotrörelse i en specialtillverkad rygg modell, på friska försökspersoner samt på två mindre grupper av patienter, en grupp som hade opererats i nacken och hade diskproteser och en annan grupp som vi studerade före och efter diskprotes kirurgi i ländryggen. Vi undersökte de friska försöks personerna och patienterna i framåtböjning respektive bakåtböjning av ryggen. Vi analyserade de segmentella rörelserna i länd-och halsryggen med sk stelkropps transformation. Denna analysmetod har utvecklats av vår forskargrupp.

Resultat: I ländryggen var mätnoggrannheten 0,6 mm för glidrörelse och ca 1 grad för rotation i modellen studien. Visuellt upptäcktes rörelser som översteg 1 mm. Upprepbarheten i mätningarna på friska försökspersoner var 2,8 grader i rotation och 1,8 mm i glidrörelse. Facettledens 3D-rörelsen var cirka 6 mm i L4-L5 och 5 mm L5-S1. Segmentell rotation i sagittal planet var ca 14 grader i L4-L5 och ca 10 grader i L5-S1. Patienter med diskprotes hade i snitt 5 grader rotation innan operation i den opererade nivåen (L5-S1) och ca 7 grader efter operation. I den intilliggande nivån (L4-L5) var rotationen i snitt ca 8 grader före och 9 grader efter operation. 3D glidningen av facettleder i det opererade nivån var cirka 4 mm före och efter operation. I den intilliggande nivån var 3D glidningen av facettlederna var ca 4 mm före och efter operation. I halsryggen noggrannhet var 0,7 grader i rotation och 0,5 mm i glidrörelse i modellen. Upprepbarheten på modellen var 1,1 grader i rotation och 0,3 mm i glidrörelse Upprepbarheten på patienter var 2,3 grader i rotation och 1,4 mm i glidrörelse.

Slutsats: Vi har utvecklat en icke-invasiv CT baserad metod för att studera 3D segmentell rörelse i ryggraden. Den har testats i en modell studie, på friska försökspersoner och på patienter. Denna metod lämpar sig väl för att utvärdera den segmentella rörligheten i ryggraden. Vår metod är därför användbar både kliniskt och för forskning i syfte att undersöka patienter med kvarstående besvär efter steloperation och för att undersöka den biomekaniska funktionen efter olika implantat i ryggen.

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